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EXAMINER	
BRUMBACK, B	
BRENDA BRUMBACK	
ART UNIT	PAPER NUMBER
1642	15

DATE MAILED: 03/30/00

Below is a communication from the EXAMINER in charge of this application

COMMISSIONER OF PATENTS AND TRADEMARKS

ADVISORY ACTION

☑ THE PERIOD FOR RESPONSE:

a) ☑ is extended to run 5 months ~~or continues to run~~ _____ from the date of the final rejection

b) ☐ expires three months from the date of the final rejection or as of the mailing date of this Advisory Action, whichever is later. In no event however, will the statutory period for the response expire later than six months from the date of the final rejection.

Any extension of time must be obtained by filing a petition under 37 CFR 1.136(a), the proposed response and the appropriate fee. The date on which the response, the petition , and the fee have been filed is the date of the response and also the date for the purposes of determining the period of extension and the corresponding amount of the fee. Any extension fee pursuant to 37 CFR 1.17 will be calculated from the date of the originally set shortened statutory period for response or as set forth in b) above.

☐ Appellant's Brief is due in accordance with 37 CFR 1.192(a).

☐ Applicant's response to the final rejection, filed _____ has been considered with the following effect, but it is not deemed to place the application in condition for allowance:

1. ☑ The proposed amendments to the claim and /or specification will not be entered and the final rejection stands because:

   a. ☐ There is no convincing showing under 37 CFR 1.116(b) why the proposed amendment is necessary and was not earlier presented.

   b. ☑ They raise new issues that would require further consideration and/or search. (See Note).

   c. ☑ They raise the issue of new matter. (See Note).

   d. ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal.

   e. ☐ They present additional claims without cancelling a corresponding number of finally rejected claims.

   NOTE: See attached.

2. ☐ Newly proposed or amended claims _____ would be allowed if submitted in a separately-filed amendment cancelling the non-allowable claims.

3. ☐ Upon the filing an appeal, the proposed amendment ☐ will be entered ☐ will not be entered and the status of the claims will be as follows:

   Claims allowed: _____
   Claims objected to: _____
   Claims rejected: _____

   However;

   ☐ Applicant's response has overcome the following rejection(s): _____

4. ☑ The affidavit, exhibit or request for reconsideration has been considered but does not overcome the rejection because See attached

5. ☐ The affidavit or exhibit will not be considered because applicant has not shown good and sufficent reasons why it was not earlier presented.

☐ The proposed drawing correction ☐ has ☐ has not been approved by the examiner.

☐ Other

PAULA K. HUTZELL
SUPERVISORY PATENT EXAMINER

PTOL-303 (REV. 5-89)

DETAILED ACTION

Attachment to Advisory Action

Item #1:

1. The following proposed amendments to the claims raise the issue of new matter: in claim 21 and 30, "tissue located proximate to hip bone"; in claim 31, "the area previously containing the tissue"; and in claim 33, "synthetic implant". This matter might be resolved if applicant were to point out where in the specification support for the newly recited material can be found. The section of the disclosure referenced by applicant (p. 27-p.28, "MYOTUBE TRANSFER") teaches surgically implanting myotubes into "beds of fat and connective tissues dissected and removed by surgeons" (see p. 28, lines 9-10); it does not teach implanting myotubes into the area previously containing the surgically removed tissue.

2. The following proposed amendments raise new issues under 35 U.S.C. 112, first and second paragraphs:

The proposed amendment to claim 20 reciting "an effective amount" raises a possible issue under 35 U.S.C. 112, second paragraph, because although the disclosure teaches specific numbers of 12.5 billion and 30 billion myoblast cells into diseased muscles for treatment of Duchenne muscular dystrophy (DMD) or infantile facioscapulohumeral dystrophy (IFSH), it does not teach the parameters of what other numbers are to be considered an effective amount and it does not

teach any parameters for effective numbers to be used to affect cosmetic alteration in non-diseased muscle, which is encompassed within the claimed methods.

The proposed amendment to claim 21 to add "comprises myoblasts and" and "wherein said composition fuses with the myoblasts from said body part" raises a new issue under 35 U.S.C. 112, first and second paragraphs, for recitation of breast tissue comprising myoblasts. Applicant's claims encompass adult human breast tissue. The examiner is unaware of any teaching either in applicant's disclosure or in the art that adult human breast tissue comprises myoblasts.

Item #4:

3. The rejection of claims 20-25 and 27 under 35 U.S.C. 112, first paragraph, is maintained. Applicant's arguments and attachments have been fully considered but they are not persuasive for the following reasons.

For clarification of the record, the examiner has made no statement that applicant's invention is inoperable. Rather, the claims stand rejected for lack of sufficient teachings in the disclosure to enable one of skill in the art to practice the claimed invention absent undue experimentation given the high level of unpredictability in the art.

Applicant argues that Appendix A, an apology by Dr. Eric Hoffman for damaging statements made to the media which impugned the personal character and scientific integrity of the applicant; Appendix B, a letter from the FDA designating the investigation of cultured

allogeneic myoblasts for delay or prevention of severe disability and/or death in patients with DMD; Appendix C, two of applicant's publications describing myoblast transfer for treatment of DMD; and Appendix D, which is intended to show increased muscle mass in a subject suffering from muscular dystrophy after myoblast transfer, provide evidence that MTT really works.

The relevance of Dr. Hoffman's apology to the present invention is not clear, as Dr. Hoffman makes no statements at all pertinent to cosmetic alteration of a body part. In fact, it would seem from the wording of Dr. Hoffman's apology that the damaging statements were most likely regarding a treatment for muscular dystrophy. The relevance of the FDA letter is also not clear, as it addresses investigation of myoblast transfer therapy for treating DMD. Applicant's invention is drawn to methods for cosmetic alteration of a body part and encompasses alteration of non-diseased muscle, as well as normal brest tissue. The FDA letter addresses a different subject, namely delay or prevention of disability and/or death in DMD patients. The relevance of applicant's publications describing myoblast transfer for gene therapy and treatment of DMD is also not clear, as once again they describe treatments which appear to be unrelated to the cosmetic alteration of the present invention. Lastly, Appendix D is of such poor quality that no determination can be made based on Fig. 1; however, applicant states that Fig. 1 shows cosmetic alteration of the deltoid muscle after myoblast transfer to a patient suffering from muscular dystrophy. Applicant's claimed methods, however, are for treating a body part selected from a face, a breast, a hip, and a **non-diseased** muscle (emphasis added, see claim 21). They are not drawn to treating diseased muscles from patients with muscular dystrophy. Applicant has

provided no rationale or evidence demonstrating the applicability of the method described in Appendix D to the claimed methods of cosmetically altering non-diseased tissues. Absent such evidence, Fig. 1 is not persuasive.

Additionally, all of applicant's arguments which appear on pages 4-5 regarding successful myoblast transfer therapy are directed to successful transfer for treating DMD or IFSH. None address successful transfer of myoblasts for cosmetic alteration of a breast, a hip, or a non-diseased muscle. Applicant argues that "for cosmetic treatment ... large numbers of cells make a larger difference". The examiner can find no teachings in applicant's disclosure that larger numbers of cells are needed for cosmetic treatment in support of this statement. In fact, the disclosure is silent regarding the numbers of cells to be injected for cosmetic alteration.

Applicant argues that Dimaro contains no teaching that incorporation of donor myoblasts in normal uninjured or non-diseased muscle is impossible. While it is true that Dimaro does not state that it is impossible, he does teach away from such incorporation by stating that "this observation suggests that different growth and differentiation-promoting components may regulate myoblast proliferation in developing, mature, and regenerating muscle (see page 333, first paragraph). Thus, he is suggesting that observations regarding proliferation of donor myoblasts in diseased muscles may not be applicable to normal, mature, uninjured muscle, *i.e.*, he is teaching that the art is unpredictable.

Applicant argues that the claimed invention does not require a particular degree to which donor myoblasts contribute to muscle formation. Applicant's claims recite "administering said

composition into the body part such that the cosmetic appearance of the subject is altered". Absent some evidence to the contrary, a visible alteration in a body part would seem to require a significant contribution from the donor myoblasts.

Applicant argues that breast tissue comprises myoblasts in addition to adipocytes; however, no evidence of such has been provided and the examiner is not aware of a teaching in the art that adult human breast tissue comprises myoblasts as well as adipocytes. Arguments in the absence of evidence are not persuasive.

Applicant's argument regarding avoidance of tumor formation by limiting proliferation to no more than 30 generations has been previously addressed (see paper #11, page 6, last paragraph).

Applicant argues that the examiner has improperly rejected claims 31 and 32 for lack of enablement because it would be more traumatic than prior art methods. For clarification of the record, claims 31 and 32 were rejected because the disclosure fails to provide sufficiently detailed teachings to enable the skilled artisan to practice the claimed invention absent undue experimentation. Applicant argues that the specification clearly teaches that the body part is not dissected away and reinserted after myoblast transfer, but that the claimed method removes tissue from a body part and implants myotubes into the space created by the removal. The sole referral to myotube transfer found in applicant's disclosure is at page 28, first full paragraph, which states:

> "Myotube transfer can be administered through injection with larger gauge needles. Better still, they can be surgically implanted into the beds of fat and connective

tissues dissected and removed by surgeons. Since muscles can develop greater forces and scar tissues are inert, the developing muscles will force the scar tissues aside throughout their existence."

It is certainly not clear from this paragraph that the myoblasts are injected into the space left after removal of the tissue because it is specifically stated that they are injected into the dissected tissue. Applicant's disclosure of the procedure is vague; it does not contain teachings of sufficient detail and clarity to enable the skilled artisan to practice myotube transfer for cosmetic alteration absent undue experimentation.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Brumback whose telephone number is (703) 306-3220. If the examiner can not be reached, inquiries can be directed to Supervisory Patent Examiner Paula Hutzell whose telephone number is (703) 308-4310. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Examiner Brenda Brumback, Art Unit 1642 and should be marked "OFFICIAL" for entry into prosecution history or "DRAFT" for consideration by the examiner without entry. The Art Unit 1642 FAX telephone number is (703)-305-3014. FAX machines will be available to receive transmissions 24 hours a day. In compliance with 1096 OG 30, the filing date accorded to each OFFICIAL fax transmission will be determined by the FAX machine's stamped date found on the last page of the transmission, unless that date is a Saturday, Sunday or Federal Holiday with the District of Columbia, in which case the OFFICIAL date of receipt will be the next business day.

Brenda Brumback
March 18, 2000